REMARKS

Claims 5, 10-11, 13-24, 26-28, and 36 have been amended for clarification purposes. Applicant asserts that the amendments do not raise new issues or matter. Upon entrance of the amendments, claims 3, 5-29, 35, and 36 will be pending in the captioned application. Alternately, the amendments should be considered to place the case in better form for consideration on appeal. Entrance of the amendments and further examination and reconsideration of claims 3, 5-29, 35, and 36 are respectfully requested.

Improper Final Rejection

Under present practice, second or any subsequent actions on the merits shall be final, except where the examiner introduces a new ground of rejection that is neither necessitated by applicant's amendment of the claims nor based on information submitted in an information disclosure statement filed during the period set forth in 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p). MPEP 706.07(a).

In the Final Office Action, the Examiner introduces new grounds of rejections based on U.S. Patent Application Publication Nos. 2003/0022182 by Barany et al. (hereinafter "Barany '182") and 2003/0032016 by Barany et al. (hereinafter "Barany '016") and combinations of other cited art with each of Barany '182 and Barany '016. However, these new grounds of rejection could not have been necessitated by Applicant's amendment of the claims in the Amendment; Response to Office Action Mailed April 21, 2004, which was filed in the present case on July 21, 2004 (hereinafter "the prior response"). In particular, the amendments to the claims presented in the prior response were made to correct antecedent problems and other informalities in the claims, of which at least some were specifically noted in the objections and rejections of the claims that were made in the Office Action mailed April 21, 2004. Therefore, the amendments to the claims did not necessitate new grounds of rejection. In addition, the new grounds of rejection are not based on information submitted in an information disclosure statement.

For at least the reasons set forth above, the finality of the instant Office Action is improper. Accordingly, withdrawal of the finality of the instant Office Action is respectfully requested.

Objections to the Claims

Claim 10 was objected to because of informalities. Applicant has amended this claim as suggested in the Final Office Action to correct the informalities identified in the Final Office Action. Accordingly, removal of the objections to claim 10 is respectfully requested.

Section 112, second paragraph, Rejections

Claims 5, 6, 10-29, 35, and 36 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Final Office Action points out different phrases in claims 5, 10, 15, 17, 20, 22, 23, and 24 that the Examiner contends render these claims vague and indefinite. To expedite prosecution, Applicant has amended these claims to alter the phrases indicated in the Final Office Action. The amendments to these claims are believed to address the asserted indefiniteness of these phrases. Accordingly, removal of the § 112, second paragraph, rejections of claims 5, 6, 10-29, 35, and 36 is respectfully requested.

Section 102 Rejections

Claims 3, 7, and 9 were rejected under 35 U.S.C. § 102(e) as being anticipated by Barany '182. Claim 5 was rejected under 35 U.S.C. § 102(e) as being anticipated by Barany '016. Claims 10-14, 22, 25, 26, 29, 35, and 36 were rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,355,431 to Chee et al. (hereinafter "Chee"). As will be set forth in more detail below, the § 102 rejections of claims 3, 5, 7, 9-14, 22, 25, 26, 29, 35, and 36 are respectfully traversed.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987), MPEP § 2131. The cited art does not disclose all limitations of the currently pending claims, some distinctive limitations of which are set forth in more detail below.

The cited art does not teach ligating hybridized free probes with hybridized spectrally-addressable bound probes. Independent claim 3 recites in part: "ligating the hybridized free probes with the hybridized spectrally-addressable bound probes." Amended independent claims 5 and 10 recite similar limitations.

Barany '182 discloses detection of nucleic acid sequence differences using the ligase detection reaction with addressable arrays. Barany '182, however, does not disclose ligating hybridized free probes with hybridized spectrally-addressable bound probes. For example, Barany '182 states that "The next phase of the process is the capture phase. This phase involves providing a solid support with capture oligonucleotides immobilized at particular sites." (Barany '182 -- paragraph 0029). In addition, Barany '182 states that "The mixture, after being subjected to the ligation phase, is contacted with the solid support under conditions effective to hybridize the addressable array-specific portions to the capture oligonucleotides in a base-specific manner." (Barany '182 -- paragraph 0029). Therefore, Barany '182 teaches that after ligation, the ligation product is bound to capture probes on a solid support. As such, the probes of Barany '182 that are involved in ligation are not bound until after the ligation is complete. Consequently, Barany '182 does not teach ligating hybridized free probes with hybridized spectrally-addressable bound probes, as recited in claims 3, 5, and 10. As a result, Barany '182 does not teach all limitations of claims 3, 5, and 10.

Barany '016 discloses detection of nucleic acid sequence differences using coupled ligase detection and polymerase chain reactions. Barany '016, however, does not disclose ligating hybridized free probes with hybridized spectrally-addressable bound probes. For example, Barany '016 states that "In the LDR reaction, each allele-specific probe can ligate to its adjacent fluorescently labeled common probe in the presence of the corresponding target sequence. Ligation product sequences corresponding to wild type and mutant alleles are captured on adjacent addresses on the array." (Barany '016 -- paragraph 0109). Therefore, like Barany '182, Barany '016 discloses that after ligation, the ligation product is bound to capture probes. As such, the probes of Barany '016 that are involved in ligation are not bound until after ligation is complete. Consequently, Barany '016 does not teach ligating hybridized free probes with hybridized spectrally-addressable bound probes, as recited in claims 3, 5, and 10. As a result, Barany '016 does not teach all limitations of claims 3, 5, and 10.

Chee discloses detection of nucleic acid amplification reactions using bead arrays. Chee, however, does not disclose ligating hybridized free probes with hybridized spectrally-addressable bound probes. For example, Chee states that "An immobilized first OLA primer 45 is hybridized with a target sequence 25 and a second OLA primer 50." (Chee -- col. 6, lines 61-63.) As shown in FIGS. 7A and 7B of Chee, target sequence 25 is hybridized with bound OLA primer 45. However, Chee does not teach that bound OLA primer 45 is spectrally-addressable. In addition, Chee provides no reason for the bound OLA primer to be spectrally-addressable. In particular, Chee states that "an immobilized primer is contacted with a target nucleic acid. Complementary sequences will hybridize with each other resulting in an immobilized duplex. A second primer is contacted with the target nucleic acid. The second primer hybridizes to the target nucleic acid adjacent to the first primer. An OLA assay is performed as described above." (Chee -- col. 19, lines 27-33). In addition, Chee states that "Following ligation of the oligonucleotides, the ligated, immobilized, oligonucleotide is then hybridized with an RCA probe." (Chee -- col. 19, lines 36-38). Chee also states that "Following RCA, the amplified product nucleic acid is detected (FIG. 6). This can be accomplished in a variety of ways; for example, the polymerase may incorporate labelled nucleotides, or alternatively, a label probe is used that is substantially complementary to a portion of the RCA probe and comprises at least one label is used." (Chee -- col. 19, lines 62-67). As such, Chee discloses detecting the RCA product using labeled polymerase or a labeled capture probe. Consequently, since the OLA product is not detected in this method, Chee provides no reason for the immobilized first OLA primer described above to be spectrally-addressable. Therefore, Chee does not teach ligating hybridized free probes with hybridized spectrally-addressable bound probes.

In another example, Chee states that "a target nucleic acid is added to a reaction mixture that comprises the necessary amplification components, and a modified primer is formed. In general, the modified primer comprises a detectable label, such as a fluorescent label, which is either incorporated by the enzyme or present on the original primer." (Chee – col. 7, lines 28-33.) Therefore, Chee discloses that a target nucleic acid may be contacted with a primer that includes a detectable label. However, Chee does not teach that such a primer is bound.

In a further example, Chee states that "the ligation product can be detected in a variety of ways...only one of the primers carries a detectable label, e.g. the first ligation probe, and the capture probe on the bead is substantially complementary to the other probe, e.g. the second ligation probe. In this way, unextended labeld [sic] ligation primers will not interfere with the assay" (Chee -- col. 18, lines 35-42.) Therefore, Chee discloses that one primer can carry a detectable label, but Chee does not teach that this

primer is also bound. Instead, Chee teaches that a capture probe is used to immobilize the ligation product. As such, Chee does not teach ligating hybridized free probes with hybridized spectrally-addressable bound probes, as recited in claims 3, 5, and 10. Consequently, Chee does not teach all limitations of claims 3, 5, and 10.

For at least the aforementioned reasons, claims 3, 5, and 10 are not anticipated by the cited art. Therefore, claims dependent therefrom are also not anticipated by the cited art for at least the same reasons. Accordingly, removal of the § 102 rejections of claims 3, 5, 7, 9-14, 22, 25, 26, 29, 35, and 36 is respectfully requested.

Section 103(a) Rejections

Claim 6 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Barany '016 in view of U.S. Patent No. 5,945,283 to Kwok et al. (hereinafter "Kwok"). Claim 8 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Barany '182 in view of U.S. Patent No. 6,485,944 to Church et al. (hereinafter "Church"). As will be set forth in more detail below, the §103(a) rejections of claims 6 and 8 are respectfully traversed.

To establish *prima facie* obviousness of a claimed invention, all claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974), MPEP 2143.03. Obviousness cannot be established by combining or modifying the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion or incentive to do so. *In re Bond*, 910 F. 2d 81, 834, 15 USPQ2d 1566, 1568 (Fed. Cir. 1990). The cited art does not teach or suggest all limitations of the currently pending claims, some distinctive limitations of which are set forth in more detail below.

The cited art does not teach or suggest ligating hybridized free probes with hybridized spectrally-addressable bound probes, as recited in claims 3 and 5. As set forth in more detail above, Barany '016, Barany '182, and Chee do not teach all limitations of claims 3 and 5.

Barany '016, Barany '182, and Chee also cannot be combined with Kwok and/or Church to overcome the deficiencies therein. For example, Kwok discloses methods and kits for nucleic acid analysis using fluorescence resonance energy transfer. However, Kwok does not teach or suggest ligating

hybridized free probes with hybridized spectrally-addressable probes. In particular, Kwok states that "The oligonucleotide ligation assay involves hybridization of a DNA sequence to two probes, one of which is labeled." (Kwok – col. 1, lines 48-49.) Therefore, Kwok teaches contacting a DNA sequence with a labeled probe. However, Kwok does not teach that the labeled probe is also bound. Therefore, Kwok does not teach ligating hybridized free probes with hybridized spectrally-addressable bound probes, as recited in claims 3 and 5. Consequently, Kwok does not teach all limitations of claims 3 and 5 and cannot be combined with Barany '016, Barany '182, Chee, or any combination thereof to overcome deficiencies therein.

Church discloses replica amplification of nucleic acid arrays. However, Church does not teach or suggest ligating hybridized free probes with hybridized spectrally-addressable probes. For example, Church states that "The invention provides a method for determining the nucleotide sequence of the features of an immobilized nucleic acid array, such method comprising the steps of: a) ligating a first double-stranded nucleic acid probe to one end of a nucleic acid feature of said array." (Church – col. 3, lines 40-44). In addition, Church states that "It is further preferred that each of the components of the probe is labeled with a different fluorescent dye and that the different fluorescent dyes are spectrally resolvable." (Church – col. 4, lines 4-7). Therefore, Church teaches ligating a bound nucleic acid feature with a labeled nucleic acid probe. However, Church does not teach or suggest that the bound nucleic acid is spectrally-addressable or that the labeled nucleic acid probe is bound. As such, Church does not teach or suggest performing ligation with hybridized spectrally-addressable bound probes. Therefore, Church does not teach or suggest ligating hybridized free probes with hybridized spectrally-addressable bound probes, as recited in claims 3 and 5. Consequently, Church does not teach all limitations of claims 3 and 5 and cannot be combined with Barany '016, Barany '182, Chee, Kwok, or any combination thereof to overcome deficiencies therein.

Therefore, none of the cited art, either individually or in any combination thereof, teaches, suggests, or provides motivation for ligating hybridized free probes with hybridized spectrally-addresssable bound probes, as recited in claims 3 and 5. Consequently, the cited art does not teach, suggest, or provide motivation for all limitations of claims 3 and 5.

For at least the reasons stated above, claims 3 and 5 are patentably distinct over the cited art. Therefore, claims 6 and 8, which are dependent from claims 3 and 5, respectively, are also patentably distinct over the cited art for at least the same reasons. Accordingly, removal of the § 103(a) rejections of claims 6 and 8 is respectfully requested.

CONCLUSION

This response constitutes a complete response to all issues raised in the Final Office Action mailed November 30, 2004. In view of the remarks traversing rejections presented therein, Applicant asserts that pending claims 3, 5-29, 35, and 36 are in condition for allowance. If the Examiner has any questions, comments, or suggestions, the undersigned earnestly requests a telephone conference.

The Commissioner is authorized to charge any fees which may be required, or credit any overpayment, to deposit account number 50-3268/5868-03401.

Respectfully submitted,

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